

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference SCB/53202001	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 00/ 04918	International filing date (day/month/year) 26/05/2000	(Earliest) Priority Date (day/month/year) 29/06/1999
Applicant JANSSEN PHARMACEUTICA N.V.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 9 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☒ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☒ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-5,7-46 (all partially); 6 (completely)

A nucleic acid according to SEQ ID NOs 5, 6 or 7 encoding a rat GDNF family receptor alpha-4 (rGFRalpha-4) according to SEQ ID NOs 8 or 9 or encoding a functional equivalent, and said encoded GFRalpha-4 proteins. Hybridizing nucleic acid molecules, vectors, hosts, transgenic cells, tissues or organisms, and pharmaceutical compositions. Agonists, antagonists and ligands, methods for their identification and use thereof. Antibodies and their use. Kits.

2. Claims: 1-5,7-46 (all partially)

A nucleic acid encoding a mouse GDNF family receptor alpha-4 (mGFRalpha-4) which is a functional equivalent of the receptor encoded by SEQ ID NOs 8 or 9, and said encoded mGFRalpha-4 protein. Hybridizing nucleic acid molecules, vectors, hosts, transgenic cells, tissues or organisms, and pharmaceutical compositions. Agonists, antagonists and ligands, methods for their identification and use thereof. Antibodies and their use. Kits.

3. Claims: 1-5,7-46 (all partially)

A nucleic acid encoding a human GDNF family receptor alpha-4 (hGFRalpha-4) which is a functional equivalent of the receptor encoded by SEQ ID NOs 8 or 9, and said encoded hGFRalpha-4 protein. Hybridizing nucleic acid molecules, vectors, hosts, transgenic cells, tissues or organisms, and pharmaceutical compositions. Agonists, antagonists and ligands, methods for their identification and use thereof. Antibodies and their use. Kits.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 24, 25, 31-35

Remark (2): Claims 24, 25, and 31-35 refer to agonists and/or antagonists of the polypeptide(s) without giving a true technical characterisation. Moreover, no specific compounds are defined in the application. In consequence, the scope of said claims is ambiguous and vague, and their subject-matter is not sufficiently disclosed and supported (Art. 5 and 6 PCT). No search can be carried out for such purely speculative claims whose wording is, in fact, a mere recitation of the results to be achieved.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 00/ 04918

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

On line 1 delete "novel" before "mammalian"

IN NATIONAL SEARCH REPORT

International Application No

PCT/EP 00/04918

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C12N15/12 C07K14/71 C12Q1/68 A61K38/17
A61K48/00 G01N33/50

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07K C12Q A61K G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, STRAND, EMBL, MEDLINE, WPI Data, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	THOMPSON J ET AL.: "GFRalpha-4, a new GDNF family receptor" MOLECULAR AND CELLULAR NEUROSCIENCE, vol. 11, no. 3, June 1998 (1998-06), pages 117-126, XP000960388 cited in the application	1,3-5, 7-21,36
Y	the whole document	22,23, 26-29, 37-40, 43-46
	--- -/--	



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

17 November 2000

Date of mailing of the international search report

04/12/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

van de Kamp, M

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	ENOKIDO Y ET AL.: "GFRalpha-4 and the tyrosine kinase Ret form a receptor complex for persephin" CURRENT BIOLOGY, vol. 8, no. 18, 10 September 1998 (1998-09-10), pages 1019-1022, XP000960386 cited in the application the whole document page 1019, right-hand column, line 12-14 ---	1,3-5, 7-17,21, 24-35, 38-44,46
X	DATABASE EMBL 'Online! EMBL; ID AU035938, AC AU035938, 8 October 1998 (1998-10-08) HASHIMOTO K ET AL.: "Mus musculus brain cDNA, clone MNCb-1073 : 5' end" XP002152925 cited in the application the whole document ---	1-5, 7-19,21, 36
X	DATABASE EMBL 'Online! EMBL; ID AA823200, AC AA823200, 18 February 1998 (1998-02-18) MARRA M ET AL.: "vw41h08.r1 Soares mouse mammary gland NbMMG Mus musculus cDNA clone IMAGE:1246431 5', mRNA sequence" XP002152926 cited in the application the whole document ---	1-5, 7-19,21, 36
X	WO 99 14235 A (MILBRANDT JEFFREY D ;DESAUVAGE FRED (US); KLEIN ROBERT (US); UNIV) 25 March 1999 (1999-03-25) the whole document ---	24,25, 31-35, 41,42
Y	WO 97 33912 A (GENENTECH INC ;RYAN ANNE M (US); KLEIN ROBERT D (US); MOORE MARK W) 18 September 1997 (1997-09-18) the whole document ---	22,23, 26-29, 37-40, 43-46
A	AIRAKSINEN M S ET AL.: "GDNF family neurotrophic factor signaling: four masters, one servant?" MOLECULAR AND CELLULAR NEUROSCIENCE, vol. 13, no. 5, May 1999 (1999-05), pages 313-325, XP000960431 cited in the application the whole document page 321, right-hand column, line 33-36 figures 1,2 --- -/--	1-46

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	SAARMA M ET AL.: "Other neurotrophic factors: Glial cell line-derived neurotrophic factor (GDNF)" MICROSCOPY RESEARCH AND TECHNIQUE, vol. 45, no. 4-5, 1 June 1999 (1999-06-01), pages 292-302, XP000960924 abstract page 294, right-hand column, line 57-61 figure 2	1-46
P,X	WO 99 50298 A (MILLENNIUM PHARMACEUTICALS INC) 7 October 1999 (1999-10-07) the whole document	1-5, 7-23, 26-30, 36-40, 43-46
P,X	DATABASE EMBL 'Online! EMBL; ID AF155960, AC AF155960, 28 July 1999 (1999-07-28) GUNN T M ET AL.: "Mus musculus recombination breakpoint containing region" XP002152927 cited in the application the whole document -& GUNN T M ET AL.: "The mouse mahogany locus encodes a transmembrane form of human attractin" NATURE, vol. 398, no. 6723, 11 March 1999 (1999-03-11), pages 152-156, XP002152923 page 153, right-hand column, line 11-14	1-5,7,8, 21
X		1-5, 7-21,36
Y		22,23, 26-29, 37-40, 43-46
P,X	WO 00 05373 A (MILLENNIUM PHARMACEUTICALS INC) 3 February 2000 (2000-02-03) page 87, line 30 -page 88, line 17 figure 3A figure 3D --- -/--	1-5,7,8, 21

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>DATABASE EMBL 'Online! EMBL; ID AW528607, AC AW528607, 8 March 2000 (2000-03-08) SOARES M B: "UI-R-B01-ajr-c-09-0-UI.sr UI-R-B01 Rattus norvegicus cDNA clone, UI-R-B01-ajr-c-09-0-UI 3', mRNA sequence" XP002153002 the whole document</p>	1-5,7,8, 21
X	<p>-& BONALDO M F ET AL.: "Normalization and subtraction: two approaches to facilitate gene discovery" GENOME RESEARCH, vol. 6, no. 9, September 1996 (1996-09), pages 791-806, XP002039972 abstract</p>	1-5,7
P,X	<p>--- DATABASE EMBL 'Online! EMBL; ID MMU276872, AC AJ276872, 1 May 2000 (2000-05-01) AIRAKSINEN M S: "Mus musculus mRNA for GDNF family receptor alpha 4, putative secreted isoform (Gfra4 gene)" XP002152928 the whole document</p>	1-5,7,8, 21
T	<p>-& LINDAHL M ET AL.: "Expression and alternative splicing of mouse Gfra4 suggest roles in endocrine cell development" MOLECULAR AND CELLULAR NEUROSCIENCE, vol. 15, no. 6, June 2000 (2000-06), pages 522-533, XP000960392 the whole document</p>	1-5,7,8, 18,19,21
T	<p>--- MASURE S ET AL.: "Mammalian GFRA-4, a divergent member of the GFRA family of coreceptors for GDNF family ligands, is a receptor for the neurotrophic factor persephin" JOURNAL BIOLOGICAL CHEMISTRY (JBC PAPERS IN PRESS), 24 August 2000 (2000-08-24), XP002152924 Published as Manuscript M003867200 the whole document</p>	1-46
T	<p>--- DATABASE EMBLNEW 'Online! EMBL; ID AF253318, AC AF253318, 26 October 2000 (2000-10-26) ZHOU B ET AL.: "Homo sapiens GFR receptor alpha 4 protein (GFRA4) mRNA, complete cds" XP002152929 the whole document</p>	1-5,7,8, 21

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 00/04918

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9914235 A	25-03-1999	AU 9483898 A EP 1009768 A	05-04-1999 21-06-2000
WO 9733912 A	18-09-1997	AU 719482 B AU 2217297 A CA 2246768 A EP 0888385 A ZA 9702235 A	11-05-2000 01-10-1997 18-09-1997 07-01-1999 14-09-1998
WO 9950298 A	07-10-1999	AU 3206899 A	18-10-1999
WO 0005373 A	03-02-2000	AU 5118399 A	14-02-2000